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Spontaneous assembly of a hydrogen-bonded tetrahedron

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Received (in Columbia, MO, USA) 17th July 2002, Accepted 21st August 2002
First published as an Advance Article on the web 10th September 2002

Triphenylamine *ortho*-tricarboxylic acid (1) has been synthesized and the crystal structure reported. This molecule is shown to spontaneously self-assemble into a hydrogen-bonded tetrahedron. Furthermore, Electrospray Ionization Mass Spectroscopy shows evidence for the stability of such aggregates from an ethanol/water solution.

The assembly of molecular components into discrete regular (Platonic) and semiregular (Archimedean) polyhedra *via* supramolecular interactions has received substantial attention in recent years.[1] The interest in this area stems mainly from the desire to rationalize and mimic various naturally occurring discrete high-symmetry structures such as those found in viruses and in proteins.[2] Furthermore, since these structures have cavities that can encapsulate guest molecules, applications such as catalysis and drug delivery have also been envisaged.[3] A review of supramolecular systems based on polyhedral structures has recently been published by Atwood.[4] The tetrahedron, with four vertices and six edges, belongs to a family of five regular polyhedra collectively called the Platonic solids. In 1975, Lehn and Graf reported a macrotricyclic host that was the first covalent rendition of a tetrahedron.[5] Subsequently, several examples have appeared in the literature that use metal–ligand coordination bonds to assemble molecules into a tetrahedron.[6] However, we found that the clathrate compounds of quinol[7] and triphenylmethanol[8] were the only examples that exist for the assembly of a tetrahedron through hydrogen bonds. Our research group is interested in the directed assembly of electroactive solids into targeted topologies. In this regard, we recently reported the assembly of di- and triarylamine *ortho*-dicarboxylic acids into zig-zag and helical topologies.[9] We report here the spontaneous assembly of the triphenylamine *ortho*-tricarboxylic acid **1** (Fig. 1) into a tetrahedron through hydrogen bonding.

The methyl ester derivative of **1** (*i.e.* R = CO_2Me) can be synthesized by the copper-catalyzed Ullmann coupling of methyl anthranilate and methyl 2-iodobenzoate.[10] Alternatively, this compound can be synthesized by a new methodology for amination reactions using a well-defined copper catalyst, previously reported by our group.[11] Once synthesized, the tri-*ortho*-phenyl ester can be easily hydrolyzed with sodium hydroxide in a water/ethanol solution to give **1** in almost quantitative yield. Recrystallization from a solution of ethanol/water gave small, but well-defined, colorless cubic crystals in 62% yield. Concentration of the filtrate and subsequent recrystallization gave a second crop of crystals for an overall yield of 93%.

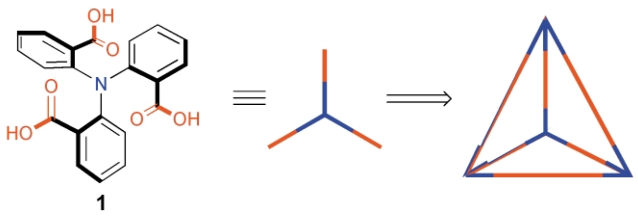

Fig. 1 Schematic representation of **1** as a tetrahedral synthon.

Single crystal X-ray diffraction† shows that **1**‡ assembles into tetrahedral clusters (Fig. 2). These clusters are held together by hydrogen-bonding interactions, however, it is not the usual dimeric interaction commonly observed for carboxylic acid moieties.[12] Instead, the acid groups are partially bonded to each other and partially bonded to a 3-fold disordered ethanol molecule that is present in the center of each face of the tetrahedral cluster. The secondary carbon of each ethanol molecule lies on the 3-fold symmetry axis. When connected, these carbons form a second tetrahedron within the larger tetrahedron, but with opposite geometry.[13] Both of the tetrahedral clusters have the typical dimensions of a perfect tetrahedron, namely 60° inner angles. However, the angles between the carbon–nitrogen bonds of the triarylamines occupying the vertices of the outer cluster are 118°, which deviates from the ideal tetrahedral angles of 109.5° but are consistent with the carbon–nitrogen–carbon bond angles of 120° observed for triphenylamine. The sides of the outer and inner clusters are 9.7 Å and 4.4 Å, respectively.

Although there are no hydrogen-bond interactions between these tetrahedral clusters, they do self-organize to form a secondary structure, namely a cubic packing motif. Fig. 3 shows that the tetrahedra pack in a motif that is geometrically body-centered cubic (bcc) with each side of the cube being 15.8 Å in length. Symmetrically, the packing would be more accurately described as two interpenetrated simple cubes. Although common for inorganic systems, cubic space groups are relatively unusual for purely organic systems. In fact, a search of the Cambridge Structural Database shows that less than 0.1% of all the reported organic compounds there are cubic. This crystal structure was reproducible over multiple recrystallizations. Attempts to incorporate larger alcohols, like isopropanol, resulted in open structures.

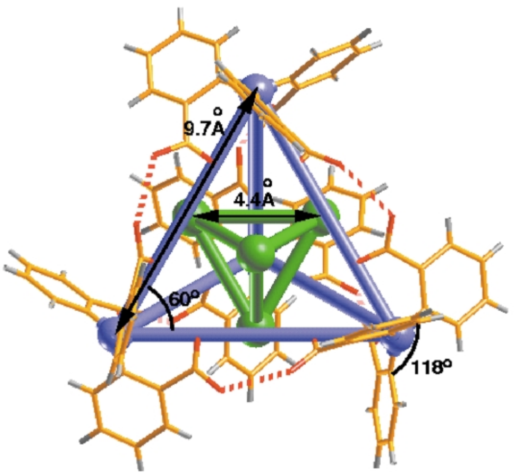

Fig. 2 Illustration of the supramolecular structure of **1** from single crystal X-ray diffraction. Nitrogen atoms (blue) and the secondary carbons of the ethanol molecules (green) are connected to show the tetrahedral cluster and solvent ordering. The closest carbonyl oxygens have been connected (red dashed) however, the disordered hydrogen-bonded atoms have been removed for clarity.

DOI: 10.1039/b207026j

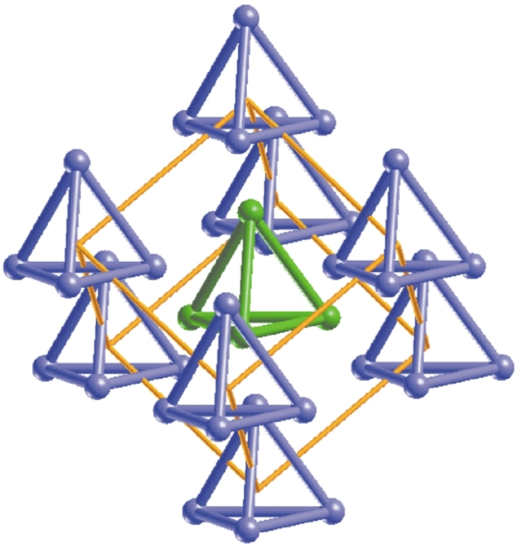

Fig. 3 Illustration of the bcc-like packing motif of the supramolecular tetrahedra of **1** from single crystal X-ray diffraction. The center tetrahedron (green) is surrounded by 8 other tetrahedra (blue) that occupy the corners of the body-centered cube (orange).

Having established the tetrahedral hydrogen-bonded structure in the solid state, we decided to investigate the stability of this species in solution.§ Electrospray ionization mass spectrometry (ESI-MS) has been previously used to characterize similar stable non-covalent aggregates in solution.[14] Fig. 4 shows the ESI mass spectrum of **1**¶ in a solution of 20% water in ethanol. As can be seen, the peak at *m*/*z* 1531.6 is predominant and corresponds to an $[M_4 + Na]^+$ aggregate, presumably the tetrahedral cluster. This is an indication of the intrinsic stability of the tetrahedral structure. Also present in small amounts are peaks at *m*/*z* 399.9 and 1155.1 corresponding to $[M + Na]^+$ and the doubly charged $[M_6 + 2Na]^{2+}$, respectively. It is also interesting to note that solutions of **1** in pure ethanol show predominately the molecular ion peak, even though the solid-state structure shows no evidence of water participating in the hydrogen-bonded structure. Water concentrations above 20% gave cluttered spectra with additional peaks corresponding to M_2 and M_3 aggregates as well as M_4 aggregate peaks with incorporated water molecules.

In summary, we have reported a purely organic, hydrogen-bonded, supramolecular tetrahedral structure based on molecule **1**. Moreover, the ethanol solvent molecules are intrinsically ordered in a tetrahedral fashion within this structure. It may be possible to exploit the structural characteristics of this system along with the well-documented electronic properties of triarylamines,[15] in order to assemble new materials with interesting solid-state properties. Research towards this end is underway and will be reported in due course.

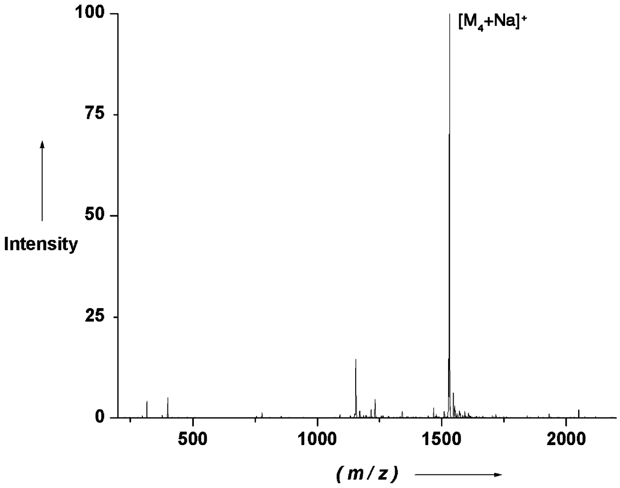

Fig. 4 The electrospray ionization (ESI) mass spectrum of **1** in a 1 : 5 water/ethanol solution. The peak at *m*/*z* 1531.6 corresponds to the $[M_4 + Na]^+$ aggregate.

Financial support for this research was provided by the University of Massachusetts, Amherst start-up funds and the National Science Foundation CAREER grant CHE-0134287. We thank the X-ray Structural Characterization Laboratory supported by National Science Foundation grant CHE-9974648 for assistance with the crystallographic analyses.

Notes and references

† X-Ray data were collected using a Nonius kappa-CCD diffractometer with MoKα (λ = 0.71073 Å) as the incident radiation. Structures were solved using SIR97 and refined by full-matrix least-squares on F_o^2 using SHELXL97.

‡ *Crystal data* for **1**: $C_{21}H_{15}NO_6 \cdot C_2H_5OH$, M = 377.35, cubic, $P\bar{4}3n$ (no. 218), a = 15.8558(3) Å, V = 3986.25(13) Å^3, Z = 8, μ = 0.105 mm^{-1}, T = 90 K, data/parameters = 1518/91, converging to R_1 = 0.0752, wR_2 = 0.2101 (on 1327, $I > 2\sigma(I)$ observed data); R_1 = 0.0843, wR_2 = 0.2255 (all data), residual electron density: 0.43 e Å^{-3}. CCDC 186794. See http://www.rsc.org/suppdata/cc/b2/b207026j/ for crystallographic data in CIF or other electronic format.

§ The crystals remained stable in the solid state even after heating at 80 °C for 30 min.

¶ ESI-MS was carried on a Bruker Esquire-LC quadrupole ion trap mass spectrometer in positive ion mode. The capillary temperature was held at 150 °C, the capillary voltage was set at 50 V, skimmer 1 was held at 30 V, and skimmer 2 was held at 5.0 V.

1 (*a*) L. R. MacGillivray and J. L. Atwood, *J. Solid State. Chem.*, 2000, **152**, 199; (*b*) P. J. Stang and B. Olenyuk, *Acc. Chem. Res.*, 1997, **30**, 502; (*c*) D. L. Caulder and K. N. Raymond, *Acc. Chem. Res.*, 1999, **32**, 975; (*d*) D. L. Caulder and K. N. Raymond, *J. Chem. Soc., Dalton Trans.*, 1999, 1185; (*e*) M. Fujita, K. Umemoto, M. Yoshizawa, N. Fujita, T. Kusukawa and K. Biradha, *Chem. Commun.*, 2001, 509; (*f*) J. Lu, A. Mondal, B. Moulton and M. J. Zaworotko, *Angew. Chem., Int. Ed.*, 2001, **40**, 2113; (*g*) B. Moulton, J. Lu, A. Mondal and M. J. Zaworotko, *Chem. Commun.*, 2001, 863; (*h*) L. R. MacGillivray and J. L. Atwood, *Nature*, 1997, **389**, 469.
2 K. Namba and G. Stubbs, *Science*, 1986, **231**, 1401.
3 F. Hof, S. L. Craig, C. Nuckolls and J. Rebek,, *Angew. Chem., Int. Ed.*, 2002, **41**, 1488.
4 L. R. MacGillivray and J. L. Atwood, *Angew. Chem., Int. Ed.*, 1999, **38**, 1018.
5 E. Graf and J.-M. Lehn, *J. Am. Chem. Soc.*, 1975, **97**, 5022.
6 (*a*) O. D. Fox, M. G. B. Drew and P. D. Beer, *Angew. Chem., Int. Ed.*, 2000, **39**, 136; (*b*) A. J. Terpin, M. Ziegler, D. W. Johnson and K. N. Raymond, *Angew. Chem., Int. Ed.*, 2001, **40**, 157; (*c*) C. Brückner, R. E. Powers and K. N. Raymond, *Angew. Chem., Int. Ed.*, 1998, **37**, 1837; (*d*) R. L. Paul, S. M. Couchman, J. C. Jeffery, J. A. McCleverty, Z. R. Reeves and M. D. Ward, *J. Chem. Soc., Dalton Trans.*, 2000, 845.
7 O. Ermer and C. Röbke, *J. Am. Chem. Soc.*, 1993, **115**, 10077.
8 (*a*) G. Ferguson, J. F. Gallagher, C. Glidewell, J. N. Low and S. N. Scrimgeour, *Acta Crystallogr., Sect. C*, 1992, **48**, 1272; (*b*) A. E. Aliev, E. J. MacLean, K. D. M. Harris, B. M. Kariuki and C. Glidewell, *J. Phys. Chem. B*, 1998, **102**, 2165.
9 J. E. Field and D. Venkataraman, *Chem. Commun.*, 2002, 306.
10 (*a*) D. Hellwinkel and M. Melan, *Chem. Ber.*, 1971, **104**, 1001; (*b*) J. E. Field and D. Venkataraman, *Chem. Mater.*, 2002, **14**, 962.
11 R. Gujadhur, D. Venkataraman and J. T. Kintigh, *Tetrahedron Lett.*, 2001, **42**, 4791.
12 (*a*) L. Leiserowitz, *Acta Crystallogr., Sect. B*, 1976, **32**, 775; (*b*) M. C. Etter, *Acc. Chem. Res.*, 1990, **23**, 120; (*c*) G. R. Desiraju, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2311.
13 This sort of solvent ordering has been observed in other hydrogen-bonded clathrate structures, like those reported by Atwood: J. L. Atwood, L. J. Barbour, T. J. Ness, C. L. Raston and P. L. Raston, *J. Am. Chem. Soc.*, 2001, **123**, 7192 and references cited therein.
14 (*a*) X. Cheng, Q. Gao, R. D. Smith, E. E. Simanek, M. Mammen and G. M. Whitesides, *J. Org. Chem.*, 1996, **61**, 2204 and references therein (*b*) C. J. Kuehl, T. Yamamoto, S. R. Seidel and P. J. Stang, *Org. Lett.*, 2002, **4**, 913.
15 Y. Shirota, *J. Mater. Chem.*, 2000, **10**, 1.